IN THE SPECIFICATION

1. Please replace the paragraphs spanning pages 2 and 3 with the following paragraph:

An outbreak of a virulent respiratory virus, now known as Severe Acute Respiratory Syndrome (SARS), was identified in Hong Kong, China and a number of other countries around the world in 2003. Patients typically had symptoms including fever, dry cough, dyspnea, headache, and hypoxemia. Isolates of the SARS virus appear to have homology with at least the RNA polymerase gene of several known coronaviruses. A phylogenetic analysis of this homology is presented in Peiris *et al.*, "Coronavirus as a possible cause of severe acute respiratory syndrome", *Lancet,* published online April 8, 2003 at ~~*http://image.thelancet.com/extras/03art3477web.pdf*~~, *image.thelancet.com/extras/03art3477web.pdf* incorporated herein by reference in its entirety. Other sequenced fragments of the SARS virus genome appear to overlap with the open reading frame 1b of coronaviruses. See, Drosten *et al.*, "Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome", *New England Journal of Medicine*, published online at ~~*http://www.nejm.org*~~ *www.nejm.org* on April 10, 2003, incorporated herein by reference in its entirety.

The Genome Science Center in British Columbia, Canada published on its website ~~*(http://www.bcgsc.ca/bioinfo/SARS/)*~~ *(www.bcgsc.ca/bioinfo/SARS/)* a draft genome assembly of 29,736 base pairs of a virus believed to be a SARS virus, referred to as the TOR2 isolate. This draft genome assembly is given herein as SEQ ID NO: 1.

The Centers for Disease Control (CDV) published a nucleotide sequence of a SARS-CoV strain (SEQ ID NO: 2) on its website

~~*(http://www.cdc.gov/ncidod/sars/pdf/nucleoseq.pdf)*~~

(www.cdc.gov/ncidod/sars/pdf/nucleoseq.pdf). The CDC has also published a phylogenetic tree of the predicted N, S and M proteins (attached as FIGURE 6). This tree places the SARS virus outside any of the previously known coronavirus groups.

2. Please replace the second paragraph on page 17 with the following paragraph:

Severe Acute Respiratory Syndrome (SARS) virus has recently been identified as a new viral species. The SARS viral species includes the following isolates.

- two virus isolates described in Peiris *et al.* "Coronavirus as a possible cause of severe acute respiratory syndrome" *Lancet* published online at ~~*http://image.thelancet.com/extras/03art3477web.pdf*~~ *image.thelancet.com/extras/03art3477web.pdf* on April 8, 2003, incorporated herein by reference in its entirety and the sequences deposited with GenBank at accession number AY268070.
- the isolates and virual sequences described in Drosten *et al.*, "Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome", New England Journal of Medicine, published online at ~~*http://www.nejm.org*~~ *www.nejm.org* on April 10, 2003.
- the isolates and viral sequences described on the website of the WHO network on March 25 and 24, 2003
- the isolates and viral sequences described in Tsang *et al.*, "A Cluster of Cases of Severe Acute Respiratory Syndrome in Hong Kong" *New England Journal of Medicine*, published online at ~~*http://www.nejm.org*~~ *www.nejm.org* on March 31, 2003.

- the isolates and viral sequences described in Poutanen *et al.*, "Identification of Severe Acute Respiratory Syndrome in Canada" *New England Journal of Medicine*, published online at ~~*http://nejm.org*~~ *nejm.org* on March 31, 2003.

3. Please replace the third paragraph on page 19 with the following paragraph:

In one embodiment, the polynucleotides of the invention do not include one of the following five primers, disclosed at ~~*http://content.nejm.org/cgi/reprint/NEJMoa030781v2.pdf:*~~ *content.nejm.org/cgi/reprint/NEJMoa030781v2.pdf:* SEQ ID NOs:6034-38.

4. Please replace the second paragraph on page 79 with the following paragraph:

A portion of SEQ ID NO: 9968 matches with approximately 98% identity to a previously published SARS polynucleotide sequence, commonly referred to as "BNI-1" (SEQ ID NO: 10033). BNI-1 was sequenced at Bernhard Nocht Institute for Tropical Medicine, Nation Reference Center for Tropical Infectious Diseases in Hambur, Germany. The BNI-1 sequence was published on the WHO website on April 4, 2003 at ~~*http://www.who.int/csr/sars/primers/en*~~ *www.who.int/csr/sars/primers/en* and in Dorsten *et al.*, "Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome", *New England Journal of Medicine*, published online at ~~*http://www.nejm.org*~~ *www.nejm.org* on April10, 2003. Both references are incorporated herein by reference in their entirety. The six reading frames of this 302mer sequence are shown in Figure 114 (see also Figure 129). The constituent amino acid sequences from Figure 114, having at least 4 amino acids, are listed as SEQ ID NO^{s}: 10034 to 10065. An alignment of SEQ ID NO: 10034 with SEQ ID NO: 9997 is shown in Figure 130.

5. Please replace the fifth paragraph on page 85 with the following paragraph:

In one embodiment, the polynucleotides of the invention do not include one of the following primers, disclosed at

~~*http://content.nejm.org/cgi/reprint/NEJMoa030781v2.pdf:*~~

content.nejm.org/cgi/reprint/NEJMoa030781v2.pdf:

6. Please replace the fourth full paragraph spanning pages 100 and 101 with the following paragraph:

Polypeptides of the invention can be prepared in many ways *e.g.* by chemical synthesis (at least in part), by digesting longer polypeptides using proteases, by translation from RNA, by purification from cell culture (*e.g.* from recombinant expression), from the organism itself (*e.g.* after viral culture, or direct from patients), from a cell line source *etc.* A preferred method for production of peptides <40 amino acids long involves *in vitro* chemical synthesis (Bodanszky (1993) *Principles of Peptide Synthesis* (ISBN: 0387564314); Fields *et al.* (1997) *Methods in Enzymology 289: Solid-{hase Peptide Synthesis.* ISBN: 0121821900). Solid phase peptide synthesis is particularly preferred, such as methods based on t-Boc or Fmoc (Chan & White (2000) *Fmoc Solid Phase Peptide Synthesis* ISBN: 0199637245) chemistry. Enzymatic synthesis (Kullmann (1987) *Enzymatic Peptide Synthesis.* ISBN: 0849368413) may also be used in part or in full. As an alternative to chemical synthesis, biological synthesis may be used *e.g.* the polypeptides may be produced by translation. This may be carried out in vitro or in vivo. Biological methods are in general restricted to the production of polypeptides based on L-amino acids, but manipulation of translation machinery (*e.g.* of aminoacyl tRNA molecules) can be used to allow the introduction of D-amino acids (or

of other non natural amino acids, such as iodotyrosine or methylphenylalanine, azidohomoalanine, *etc.*) (Ibba (1996) *Biotechnol Genet Eng Rev* 13:197-216.). Where D-amino acids are included, however, it is preferred to use chemical synthesis. Polypeptides of the invention may have covalent modifications at the C-terminus and/or N-terminus, particularly where they are for *in vivo* administration *e.g.* by attachment of acetyl or carboxamide, as in the ~~Fuzeon™~~ FUZEON™ (enfuvirtide) product.

7.Please replace the third paragraph on page 108 with the following paragraph:

Known serum-free media include Iscove's medium, Ultra-CHO medium (~~Bio Whittaker~~ BIOWHITTAKER®) or EX-CELL (JRH Bioscience). Ordinary serum-containing media include Eagle's Basal Medium (BME) or Minimum Essential Medium (MEM) (Eagle, Science, 1330, 432 (1959)) or Dulbecco's Modified Eagle Medium (DMEM or EDM), which are ordinarily used with up to 10% fetal calf serum or similar additives. Optionally, Minimum Essential Medium (MEM) (Eagle, Science, 130, 432, (1959)) or Dulbecco's Modified Eagle Medium (DMEM or EDM) may be used without any serum containing supplement. Protein-free media like PF-CHO (JHR Bioscience), chemically-defined medial like ProCHO 4CDM (~~Bio Whittaker~~ BIOWHITTAKER®) or SMIF 7 (~~Gibco~~ GIBCO® /BRL Life Technologies) and mitogenic peptides like Primactone, Pepticase or ~~HyPep™~~ HYPEP™ (protein hydrolysate from wheat gluten)(all from Quest International) or lactalbumin hydrolzate (~~Gibco~~ GIBCO® an other manufacturers) are also adequately known in the prior art. The media additives based on plant hydrolyzates have the special advantage that contamination with viruses, mycoplasma or unknown infectious agents can be ruled out.

8. Please replace the third full paragraph on page 110 with the following paragraph:

A preferred resin for use in the invention is ~~Fractogel™ EMD~~ FRACTOGEL® EMD. This synthetic methacrylate based resin has long, linear polymer chains (so-called "tentacles") covalently attached. This "tentacle chemistry" allows for a large amount of sterically accessible ligands for the binding of biomolecules without any steric hindrance. This resin also has improved pressure stability.

Column-based liquid affinity chromatography is another preferred purification method for use in the invention. One example of a resin for use in this purification method is ~~Matrex™ Cellufine™ Sulfate~~ MATREX® CELLUFINE™ SULFATE (MCS). MCS consists of a rigid spherical (approx. 45-105 μm diameter) cellulose matrix of 3,000 Dalton exclusion limit (its pore structure excludes macromolecules), with a low concentration of sulfate ester functionality on the 6-position of cellulose. As the functional ligand (sulfate ester) is relatively highly dispersed, it presents insufficient cationic charge density to allow for most soluble proteins to adsorb onto the bead surface. Therefore the bulk of the protein found in typical virus pools (cell culture supernatants, *e.g.* pyrogens and most contaminating proteins, as well as nucleic acids and endotoxins) are washed from the column and a degree of purification of the bound virus is achieved.

9. Please replace the third paragraph on page 112 with the following paragraph:

Additional purification methods which may be used to purify inactivated SARS virus include the use of a nucleic acid degrading agent, preferably a nucleic acid

degrading enzyme, such as a nuclease having DNase and RNase activity, or an endonuclease, such as from *Serratia marcescens,* commercially available as ~~Benzonase~~TM BENZONASE®, membrane adsorbers with anionic functional groups *e.g.* ~~Sartobind~~TM SARTOBIND® or additional chromatographic steps with anionic functional groups (*e.g.* DEAE or TMAE). An ultrafiltration/diafiltration and final sterile filtration step could also be added to the purification method.

Preferably, the purification includes treatment of the SARS viral isolate with one or more nucleic acid degrading enzymes. These enzymes may be used to reduce the level of host cell nucleic acid in the viral purification process. Nucleic acid digesting enzymes for use in cell culture are known in the art and include, for example, ~~Benzonase~~TM BENZONASE®.

10. Please replace the second paragraph on page 118 with the following paragraph:

Methods of preparing split SARS virus formulations may further include treatment of the viral formulation with a DNA digesting enzyme. These enzymes may be used to reduce the level of host cell DNA in the viral purification process. DNA digesting enzymes for use in cell culture are known in the art and include, for example, ~~Benzonase®~~ BENZONASE®.

Treatment of the SARS virus formulation with a DNA digesting enzyme may occur at any time in the purification and splitting process. Preferably, however, the SARS virus formulation is treated with a DNA digesting enzyme prior to use of a detergent. Still more preferably, the SARS virus formulation is treated with a DNA digesting enzyme, such as ~~Benzonas~~ BENZONASE®, prior to treatment with a cationic

detergent, such as CTAB.

11. Please replace the third paragraph on page 112 with the following paragraph:

Additional purification methods which may be used to purify inactivated SARS virus include the use of a nucleic acid degrading agent, preferably a nucleic acid degrading enzyme, such as a nuclease having DNase and RNase activity, or an endonuclease, such as from *Serratia marcescens*, commercially available as ~~Benzonase™~~ BENZONASE®, membrane adsorbers with anionic functional groups (*e.g.* ~~Sartobind™~~ SARTOBIND®) or additional chromatographic steps with anionic functional groups (*e.g.* DEAE or TMAE). An ultrafiltreation/diafiltration and final sterile filtration step could also be added to the purification method.

13. Please replace paragraph two on page 118 with the following paragraphs:

Methods of preparing split SARS virus formulations may further include treatment of the viral formulation with a DNA digesting enzyme. These enzymes may be used to reduce the level of host cell DNA in the viral purification process. DNA digesting enzymes for use in cell culture are known in the art and include, for example, ~~Benzonase®~~ BENZONASE®.

14. Please replace paragraph three on page 118 with the following paragraphs:

Treatment of the SARD virus formulation with a DNA digesting enzyme may occur at any time in the purification and splitting process. Preferably, however, the SARS virus formulation is treated with a DNA digesting enzyme prior to use of a

detergent. Still more preferably, the SARS virus formulation is treated with a DNA digesting enzyme, such as ~~Benzonase~~ BENZONASE®, prior to treatment with a cationic detergent such as CTAB.

15. Please replace the second paragraph on page 121 with the following paragraph:

In another example, a SARS subunit vaccine may be produced as follows. SARS virus may be produced using a desired mammalian cell line on microcarrier beads in large, controlled fermentors. For example, vaccine quality African Green Monkey kidney cells (VERO cells) at a concentration of 10^5 cells/mL are added to 60 to 75 L of CMRL 1969 media, pH 7.2, in a 150 L bioreactor containing 360 g of ~~Cytodex-1~~ CYTODEX-1™ (DEAE dextran) microcarrier beads and stirred for 2 hours. Additional CMRL 1969 is added to give a total volume of 150 L. Fetal bovine serum (FBS) is added to a final concentration of 3.5%. Glucose is added to a final concentration of 3.0 g/L and glutamine is added to a final concentration of 0.6 g/L. Dissolved oxygen, pH, agitation and temperature are controlled, and cell growth, glucose, lactate and glutamine levels are monitored. When cells are in logarithmic phases usually on days 3 to 4 reached a density of about $1.0\text{-}2.5\times10^6$ cells/mL, the culture medium is drained from the fermentor and 120 L of CMRL 1969, pH 7.2 (no FBS) is added and the culture stirred for 10 minutes. The draining and filling of the fermentor is usually repeated once but could be repeated up to three times. After washing the cells, the fermentor is drained and 50 L of CMRL 1969 containing 0.1% (v/v) FBS is added. The SARS virus inoculum is added at a multiplicity of infection (m.o.i.) of 0.001 to 0.01. Trypsin may be added to promote efficient infection. Additional CMRL 1969 with 0.1% FBS is added to give a final volume of 150

L. Incubation is continued at 34 C. One viral harvest is obtained from a single fermentor lot, typically at 2-7 days post-infection. Multiple harvests from a single fermentation may also be obtained.

16. Please replace the fourth paragraph on page 122 with the following paragraph:

Alternatively, substantially pure SARS virus S protein suitable for use as an immunogen in a subunit vaccine formulation may be prepared from infected cell lysates, such as for example using a non-denaturing detergent buffer containing 1% ~~Triton~~ TRITON® X-100 and deoxycholate to lyse infected cells. The cell lysates are clarified by centrifugation and S protein is purified from the cell lysates by immunoaffinity purification. A monoclonal antibody against the S protein is generated and coupled to beads and a column is constructed with those beads. SARS-infected cell lysates are applied to the column, and the column is washed with PBS containing 0.1% ~~Triton~~ TRITON® X-100. Protein bound to the column is eluted with 0.1M glycine, pH 2.5, 0.1% ~~Triton~~ TRITON® X-100. Elution samples are buffered, such as for example, with Tris, and analyzed for the presence of protein. Fractions containing the protein are pooled and dialyzed against PBS.

As discussed above, the present invention includes isolated and purified S protein of SARS virus. In one example, the virus is grown on a vaccine quality cell line, such as VERO cells, and the grown virus is harvested. The virus harvest is filtered and then concentrated typically using tangential flow ultrafiltration using a membrane of desired molecular weight cut-off and diafiltered. The virus harvest concentrate may be centrifuged and the supernatant discarded. The pellet from the centrifugation then is

detergent extracted to solubilize the S protein, for example, by resuspending the pellet to the original harvest concentrate volume in an extraction buffer containing a detergent such as a non-ionic detergent including ~~TRITON~~ TRITON® X-100.

17. Please replace the first full paragraph on page 124 with the following paragraph:

Specifically, in one method of S protein purification, the virus harvest concentrate is centrifuged at 28,000 x g for 30 minutes at 4 C. The supernatant is discarded and the pellet resuspended in extraction buffer consisting of 10 mM Tris-HC1, pH 7.0, 150 mM NaC1, 2% (w/v) ~~Triton~~ TRITON® X-100 to the original harvest concentrate volume. Pefabloc is added to a final concentration of 5mM. The suspension is stirred at room temperature for 30 minutes. The supernatant, containing the soluble S protein, is clarified by centrifugation at 28,000 x g for 30 minutes at 4C. A TMAE—~~Fractogel~~ FRACTOGEL® column is equilibrated with 10mM Tris-HC1, pH 7.0, 150 mM NaC1 containing 0.02% ~~Triton~~ TRITON® X-100. The Triton X-100 supernatant, containing the soluble S protein, is loaded directly onto the TRAE-~~Fractogel~~ FRACTOGEL® column. The total volume added plus 2 bed volumes of 10mM Tris-HC1, pH 7.0, 150 mM NaC1 containing 0.02% ~~Triton~~ TRITON® X-100 are collected. The TMAE—~~Fractogel~~ FRACTOGEL® flow-through containing S protein is diluted 3-fold with 10 mM Tris-HC1, pH 7.0, containing 0.02% Triton X-100.

An hydroxyapatite column is equilibrated with 10 mM Tris-HC1, pH 7.0, 50 mM Nac1, 0.02% ~~Triton~~ TRITON® X-100. After loading the TMAE flow-through, the column is washed with 2 column volumes of 10 mM Tris-HC1, pH 7.0, 50mM NaC1, 0.02% Triton X-100 followed by 4 column volumes of 5 mM sodium phosphate, pH 7.0

1M NaCl, 0.02% TRITON® X-100. The proteins are eluted with 4 column volumes of 20 mM sodium phosphate, pH 7.0, 1M NaCl, 0.02% TRITON® X-100. Fractions are collected based on A280 and the protein content and antigen concentrations are measured. The purified S protein is ultrafiltered by tangential flow ultrafiltration using a 300 kDa NMWL membrane.

18. Please replace the first full paragraph on page 131 with the following paragraph:

The PCR amplification protocol was as follows: 200ng of genomic DNA from *Neisseria meningitidis* 2996 or 10 ng of plasmid DNA preparation (plasmid pCMV new, containing the entire gene coding of the Spike protein), where used as template in the presence of 40μM of each oligonucletide primer, 400-800 μM dNTPs solution, 1 x PCR buffer (including 1.5mM $Mgcl_2$), 2.5 units *TaqI* DNA polymerase (using Perkin-Elmer ~~AmpliTaQ~~ AMPLITAQ® or ~~Invitrogen~~ INVITROGEN™ ~~Platinum~~ PLATINUM® Pfx DNA polymerase).

19. Please replace the fourth full paragraph on page 131 with the following paragraph:

The purified DNA corresponding to the amplified fragment and the plasmid vectors were digested with the appropriate restriction enzymes, purified using the ~~QIAquick™~~ QIAQUICK™ PCR purification kit (following the manufacturer's instructions) and ligation reactions were performed.

20. Please replace the fifth full paragraph on page 131 with the following paragraph:

The ligation products were transformed into competent *E. coli* DH5α and

screening for recombinant clones was performed by growing randomly-selected colonies and extracting the plasmid DNA using the Qiagen ~~QIAprep~~ QIAPREP™ Spin Miniprep Kit, following the manufacturer's instructions.

21. Please replace the seventh full paragraph spanning pages 131 and 132 with the following paragraph:

Whole cell lysates were obtained resuspending bacteria in SDS-sample buffer 1X and boiling for 5-10 min. Equal amounts of proteins were separated using ~~NuPAGE~~ ~~NuPAGE®~~ (~~Invitrogen~~ INVITROGEN™) or BIORAD Gel System, according to the manufacturer's instructions. Proteins were revealed by Coomassie-blue staining or transferred onto nitrocellulose membranes for western blot analysis. Western blot was performed using a rabbit polyclonal anti-serum against purified $NadA_{\Delta 351-405}$ (diluted 1:3000) and a secondary peroxidase-conjugate antibody (DAKO).

22. Please replace the second full paragraph on page 137 with the following paragraph:

Chinese Hamster Ovary (CHO) or other eukaryotic (*e.g.,* mammalian) cells that stably express the SARS viral antigens of the invention may also be derived (*e.g.* Figure 73). Preferably, the cells are CHO cells, and these constructs will comprise one or more marker or selection genes in order to select for the desired CHO cells. In one embodiment, the constructs comprise a CMV enhancer/promoter, ampicillin resistance gene, and a fused DHFR and attenuated neomycin gene for selection purposes. Stable cell lines can then be produced using the neomycin selection system in CHOK-1 cells. Selected clones can then be sequenced to verify the integrity of the insert, and transient tranfections can then be performed using ~~Trans-LT1~~ TRANS®-LT1 polyamine

transfection reagent (PanVera Corp., Madison, WI) to assess the expression level and also the integrity of the expressed protein by ELISA and western blot analysis.

23. Please replace the first full paragraph on page 138 with the following paragraph:

The antigen capture ELISA assay for the SARS spike protein can be performed as described in the art. A brief description of this assay follows. 96 well flat-bottom plates (Corning, Corning, NY) are coated with 250ng per well of purified immunoglobulin obtained from rabbit sera that were immunized with inactivated SARS virus. Between steps, the plates are washed in a buffer containing 16%NaC1 and 1% ~~Triton~~ TRITON® X100. 100µL of supernatant or lysate samples (diluted in a buffer containing 100mM $NaPO_4$, 0.1% Casein, 1mM EDTA, 1% ~~Triton~~ TRITON® X100, 0.5M NaC1 and 0.01% Thiomersal, pH 7.5) are added and incubated for 2 hours at 37°C. Bound antigen is reacted against pooled SARS+ve serum or high affinity monoclonal antibody either human or mouse against SARS spike protein (1 hour incubation, 37°C) and detected using appropriate species-specific peroxidase conjugated second antibody (30 minute incubation at 37°C; TAGO, Burlingame, CA). The plates are developed for 15 minutes at room temperature using TMB substrate (Pierce, Rockford, IL) and the reaction stopped using 4N phosphoric acid. The plates are read at a wavelength of 450nm and the concentration of protein per ml sample is derived from a standard curve (OD *vs* protein concentration) based on serial dilutions of a know concentration of recombinant spike protein.

24. Please replace the fifth full paragraph on page 155 with the following paragraph:

Non-ionic surfactants may be used to enhance the stability of the VLP formulations of the invention. Surfactants suitable for use in vaccine formulation are known in the art and include, for example, polyoxyethylene sorbital fatty acid esters (Polysorbates) such as Polysorbate 80 (*e.g.*, ~~TWEEN 80~~ TWEEN 80®), Polysorbate 20 (*e.g* ~~TWEEN 20~~ TWEEN 20®), polyoxyethylene alkyl esters (*e.g.*, Brij 35, Brij 58), as well as others, including ~~Triton~~ TRITON® X-100, ~~Triton~~ TRITON® X-114, NP-40, Span 85 and the ~~Pluronic~~ PLURONIC® series of non-ionic surfactants (*e.g.*, ~~Pluronic~~ PLURONIC®121). The surfactant is preferably present in a concentration of from about 0.0005% to about 0.5% (wt/vol).

25. Please replace the fifth full paragraph spanning pages 163 and 164 with the following paragraph:

Particularly preferred adjuvants for use in the compositions are submicron oil-in-water emulsions. Preferred submicron oil-in-water emulsions for use herein are squalene/water emulsions optionally containing varying amounts of MTP-PE, such as a submicron oil-in-water emulsion containing 4-5% w/v squalene, 0.25-1.0% w/v ~~Tween 80™~~ TWEEN 80™ (polyoxyelthylenesorbitan monooleate), and/or 0.25-1.0% ~~Span 85™~~ SPAN®85 (sorbitan trioleate), and, optionally, N-acetylmuramyl-L-alanyl-D-isogluatminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-huydroxyphosphophoryloxy)-ethylamine (MTP-PE), for example, the submicron oil-in-water emulsion known as ~~"MF59"~~ "MF59®" (International Publication No. WO 90/14837; US Patent Nos. 6,299,884 and 6,451,325, incorporated herein by reference in their entireties; and Ott *et al.*, "MF59 – Design and Evaluation of a Safe and Potent Adjuvant for Human Vaccines"

in *Vaccine Design: The Subunit and Adjuvant Approach* (Powell, M.F. and Newman, M.J. eds.) Plenum Press, New York, 1995, pp. 277-296). MF59 contains 4-5% w/v Squalene (*e.g* 4.3%), 0.25-0.5% w/v ~~Tween-80™~~ TWEEN 80™, and 0.5% w/v ~~Span 85™~~ SPAN®85 and optionally contains various amounts of MTP-PE, formulated into submicron particles using a microfluidizer such as Model 110Y microfluidizer (Microfluidics, Newton, MA). For example, MTP-PE may be present in an amount of about 0-500 µg/dose, more preferably 0-250 µg/dose and most preferably, 0-100 µg/dose. As used herein, the term "MF59-0" refers to the above submicron oil-in-water emulsion lacking MTP-PE, while the term MF59-MTP denotes a formulation that contains MTP-PE. For instance, "MF59-100" contains 100 µg MTP-PE per dose, and so on. MF69, another submicron oil-in-water emulsion for use herein, contains 4.3% w/v squalene, 0.25% w/v ~~Tween-80™~~ TWEEN 80™, and 0.75% w/v ~~Span 85™~~ SPAN®85 and optionally MTP-PE. Yet another submicron oil-in-water emulsion is MF75, also known as SAF, containing 10% squalene, 0.4% ~~Tween-80™~~ TWEEN 80™, 5% ~~Pluronic~~ PLURONIC®-blocked polymer L121, and thr-MDP, also microfluidized into a submicron emulsion. MF75-MTP denotes an MF75 formulation that includes MTP, such as from 100-400 µg MTP-PE per dose.

26. Please replace the third paragraph on page 179 with the following paragraph:

As used herein, the term "probe" or "oligonucleotide probe" refers to a structure comprised of a polynucleotide, as defined above, that contains a nucleic acid sequence complementary to a nucleic acid sequence present in the target nucleic acid analyte. The

polynucleotide regions of probes may be composed of DNA, and/or RNA, and/or synthetic nucleotide analogs. When an "oligonucleotide probe" is to be used in a 5' nuclease assay, such as the ~~TaqMan™~~ TAQMAN™ technique, the probe will contain at least one fluorescer and at least one quencher which is digested by the 5' endonuclease activity of a polymerase used in the reaction in order to detect any amplified target oligonucleotide sequences. In this context, the oligonucleotide probe will have a sufficient number of phosphodiester linkages adjacent to its 5' end so that the 5' to 3' nuclease activity employed can efficiently degrade the bound probe to separate the fluorescers and quenchers.

27. Please replace the seventh paragraph on page 187 with the following paragraph:

One kit for amplification and detection of SARS sequences, particularly by realtime (*e.g.* ~~TaqMan™~~ TAQMAN™) PCR, uses SEQ ID NOs 6567 & 6568 as primers, and SEQ ID NO 6566 as a probe (typically labeled *e.g.* with TAMRA and/or FAM) for the amplified sequence. In some embodiments of the invention, these primers and probe are excluded.

28. Please replace the eighth paragraph on page 187 with the following paragraph:

One kit for amplification and detection of SARS sequences, particularly by realtime (*e.g.* ~~TaqMan™~~ TAQMAN™) PCR, uses SEQ ID NOs 7395 & 6568 as primers, and SEQ ID NO 6566 as a probe (typically labeled *e.g.* with TAMRA and/or FAM) for the amplified sequence. In some embodiments of the invention, these primers and probe are excluded.

29. Please replace the first full paragraph on page 285 with the following paragraph:

Computer analysis of the sequence was performed as follows. The GCG Wisconsin Package suite (version 10.0) was used for computer analysis of gene and protein sequences. The PSORT program (*~~http://psort.nibb.ac.jp/~~* *psort.nibb.ac.jp/*) was used for localization predictions. For secondary structure analysis, the PHD software available on the Web at *~~http://cubic.bioc.columbia.edu/predictprotein/~~* *cubic.bioc.columbia.edu/predictprotein/* was applied. The PSI-BLAST algorithm was used for homology searches (*~~http://www.ncbi.nlm.nih.gov/blast~~* *www.ncbi.nlm.nih.gov/blast*) using the non-redundant protein database. ClustalW was applied to obtain multiple sequence alignments of gene and protein sequences. The LearnCoil-VMF program was used to predict coiled-coil regions in the spike proteins (*~~http://learncoil-vm.lcs.mit.edu/cgi-bin/vmf~~* *learncoil-vm.lcs.mit.edu/cgi-bin/vmf*). Leucine zippers were predicted with the program 2ZIP, available at *~~http://2Zip.molgen.mpg.de~~* *2Zip.molgen.mpg.de*.

30. Please replace the second paragraph on page 292 with the following paragraph:

The amount of proteins in the purified solution after the MCS chromatography step were assessed with a bicinchoninic acid (BCA) method (Interchim) (*see e.g.* *~~http://www.piercenet.com/files/bca.pdf~~* *www.piercenet.com/files/bca.pdf*) and electrophoresis.

31. Please replace the second paragraph on page 316 with the following paragraph:

S. cerevisiae strain AD3 was transformed with pd.SARS Spike S1 #2 and single

transformants were checked for expression after depletion of glucose in the mediu. The recombinant protein was expressed at high levels in yeast, as detected by Coomassie blue staining. In particular, yeast cells were transformed with the SARS S1 expression plasmid using the ~~Invitrogen~~ INVITROGEN™ ~~Easy Comp™~~ EASY COMP™ Transformation Kit. Expression shown in Figure 57.

32. Please replace the third paragraph on page 317 with the following paragraph:

S. cerevisiae strain AD3 was transformed with pd.SARS Spike 1195 #10 and single transformants were checked for expression after depletion of glucose in the medium. The recombinant protein was expressed at high levels in yeast, as detected by Coomassie blue staining. In particular, yeast cells were transformed with the SARS 1195 expression plasmid using the ~~Invitrogen~~ INVITROGEN™ ~~Easy Comp™~~ S.c. EASY COMP™ Transformation Kit.